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SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER

WHALEY, PABLO S

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 03/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/671,546	Applicant(s) SOME ET AL.	
	Examiner Pablo Whaley	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. <u>3/9/06</u> |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

EXAMINER'S COMMENT

Examiner has agreed to send out this supplementary office action in response to a query by applicant's attorney. See attached Interview Summary. The time period for response is hereby reset to begin from the mailing date of this office action. See the Office Action Summary.

CLAIMS UNDER EXAMINATION

Claims herein under examination are Claims 1-4.

PRIORITY

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 119, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

DRAWINGS

The drawings are objected to under 37 CFR 1.83(a) because they fail to show "x axis" and "y axis" labels as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

CLAIM REJECTIONS - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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Claims 1-4 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. The claims are directed to a method of normalizing gene expression data which recite steps equivalent to mental processes. If the "acts" of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. *Schrader*, 22 F.3d at 294-95, 30 USPQ2d at 1458-59. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process (MPEP 2106.IV.B.1).

Applicant is reminded that such processes may be statutory where they recite a concrete, tangible, and useful result (i.e. a practical application). Claims which recite a physical method or an actual transformation (i.e. a "safe harbor") of data are also statutory. The instant claims result in the mathematical operation of "performing division processing...whereby the data...for the second sample are normalized," however, data need not be normalized in order to be used. Therefore the claims do not recite a safe harbor (physical step or actual transformation of data) or a concrete, tangible, and useful result. For these reasons, the claims are not statutory.

CLAIM REJECTIONS - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 3 recite a method of "normalizing gene expression data wherein, in a process for comparing gene expression quantities..., data concerning the expression quantities having been obtained for the second sample are normalized" in the preamble. As written, it appears as if there are two separate methods being claimed. Clarification is requested.

Claims 1 and 3 recite a method "in a process for comparing expression intensities" (line 2) in the preamble. It is unclear if this process for "comparing expression intensities" is an active method step or a further limitation of the claims. If so, it is unclear in what way this limitation further limits the subsequent active method steps. Claims 2 and 4 are also rejected as being dependent from Claims 1 and 3.

Claims 1 and 3, line 10, recite the limitation "indicating the data concerning the expression quantities." It is unclear if this is an actual method step or a further limitation of the claims. Clarification is requested.

Claims 1 and 3, line 10, recite the limitation "calculating a coefficient from a value of an intercept" (step ii). It is unclear in what way the "coefficient" is related to the value of an intercept. Clarification is requested.

Claims 1 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are between steps (i) and (ii), as applicant discloses a step for calculating a coefficient from a "value of an intercepts" that has not been previously determined. Clarification is requested.

CLAIM REJECTIONS - 35 USC § 102

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The following is a quotation of the appropriate paragraphs of 35 U.S.C.102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3 and 4 are rejected under 35 U.S.C. 102 (a) and (e) as being anticipated by Li et al. (US Pat. No. 6,571,005; Filed Apr. 21, 2000).

Li et al. teach methods of feature extraction and normalization algorithms for gene expression data. More specifically, Li et al. teach the following aspects of the instantly claimed invention:

- Indicating gene expression data on a coordinate system from baseline and experimental array samples (Fig. 2), which correlates to normal and abnormal cells as in instant claims 3 step (i) and 4.
- Determining the slope of a low intensity region and slope of a high intensity region (Fig. 2) and (Col. 3, lines 27-51), which correlates to calculation of a coefficient as in instant claim 3, step (ii). Note: Calculation of the slope of a line (i.e. " $\Delta y/\Delta x$ ") can be achieved given any two points on line, including an x or y intercept.
- Relating intensities between two or more arrays as a straight line with a zero y-intercept (i.e. slope = 1) and multiplication by a scaling factor (slope of the line) (Col. 3, lines 11-23), which correlates to the straight line having slope 1 of instant claim 3, step (ii).
- Performing a division process where intensity of each EST on an array was divided by the mean intensities of all ESTs on that array and multiplied by a nominal average

intensity value (Col. 3, lines 11-23), which correlates to performing a division by value of slope as in instant claim 3, step (iii).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (US Pat. No. 6,571,005; Filed Apr. 21, 2000), in view of Tseng et al. (Nucleic Acids Research, 2001, Vol. 29, No. 12, p. 2549-2557) and Quackenbush (Nature, 2002, p.496)

Li et al. teach methods of feature extraction and normalization algorithms for gene expression data. More specifically, Li et al. teach the following aspects of the instantly claimed invention:

- Indicating gene expression data on a coordinate system from baseline and experimental array samples (i.e. normal and abnormal cells) (Fig. 2), which correlates to instant claims 1 step (i), 2, 3 step (i), and 4.
- Determining the slope of a low intensity region and slope of a high intensity region (Fig. 2) and (Col. 3, lines 27-51), which correlates to calculation of a coefficient as in instant claim 1 and 3, step (ii). Note: Calculation of the slope of a line (i.e. " $\Delta y/\Delta x$ ") can be achieved given any two points on line, including an x or y intercept.
- Relating intensities between two or more arrays as a straight line with a zero y-intercept (i.e. slope = 1) and multiplication by a scaling factor (slope of the line) to make the mean of the "experiment" chip the same as that of the baseline chip (Col. 3, lines 11-23), which correlates to instant claim 1, step (ii).
- Performing a division process where intensity of each EST on an array was divided by the mean intensities of all ESTs on that array and multiplied by a nominal average intensity value (Col. 3, lines 11-23), which correlates to performing a division by value of slope as in instant claim 3.

Li et al. do not specifically recite the limitations of "points plotted on a logarithmic coordinate system" (as in instant claims 1 and 3) per se.

Tseng et al. teach methods of microarray analysis of cDNA data including quality filtering and channel normalization. More specifically, Tseng et al. teach methods of determining and graphically representing logarithmic ratios of intensity values using different genes (Fig. 2 and p. 2550, col. 2, lines 25-35).

Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the invention of Li et al. with the added step of logarithmic graphical

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representation of gene expression data as taught by Tseng et al., where the motivation would have been to produce a continuous spectrum of values for up- and down-regulated genes (Quackenbush, Nature, 2002, p. 496), resulting in the practice of the instant claimed invention with a reasonable expectation of success.

Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tseng et al. (Nucleic Acids Research, 2001, Vol. 29, No. 12, p. 2549-2557), in view of Alon et al. (Proc. Natl. Acad. Sci., 1999, Vol. 96, p. 6745-6750).

Tseng et al. teach methods of microarray analysis of cDNA data including quality filtering and channel normalization. More specifically, Tseng et al. teach the following aspects of the instantly claimed invention:

- Indicating cDNA data on a logarithmic coordinate system from multiple samples, which correlates to indicating data concerning gene expression quantities (Fig. 2, Fig. 6, and Fig. 8), as in instant claim 1 (i).
- Compute normalized log ratios (base 10) for expression data and graphically represent the data (p.2550, col. 2, lines 25-35 and Fig. 2), which correlates to calculating a coefficient and performing division processing as in instant claim 1, step (ii) and (iii).

Tseng et al. do not specifically recite the limitations of graphically representing "normal and abnormal cells" (as in instant claim 2) per se.

Alon et al. teach methods of cluster analysis of tumor and normal colon tissues using oligonucleotide arrays. More specifically, Alon et al. teach methods graphically representing gene expression values from normal and abnormal values (Fig. 1).

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Thus it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice the invention of Tseng et al. with the added step of using normal and abnormal gene expression data taught by Alon et al., where the motivation would have been to help identify families of genes and tissues based on expression patterns in the data set (p. 6749, col. 2, lines 6-10), resulting in the practice of the instant claimed invention with a reasonable expectation of success.

CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MARJORIE A. MORAN
PRIMARY EXAMINER

Marjorie A. Moran
3/15/06